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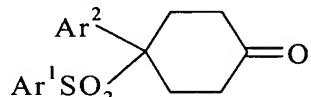
DT01 Rec'd PCT/FTC 25 JAN 2005

Amendments to the Claims:

The listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

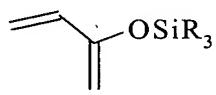
Claim 1 (Original) A method of preparing a cyclohexanone of formula (1):



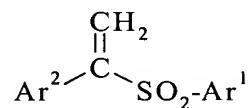
(1)

comprising:

(a) cycloaddition of a 2-trialkylsilyloxybutadiene of formula (2a) to a vinyl derivative of formula (2b):

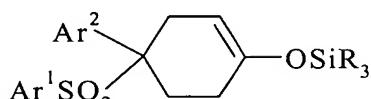


(2a)



(2b)

to form a silyl enol ether of formula (3):



(3)

and

(b) hydrolysis of said silyl enol ether to form the cyclohexanone of formula (1);

wherein, in formulae (1), (2a), (2b) and (3), R represents C₁₋₆ alkyl;

Ar¹ represents C₆₋₁₀aryl or heteroaryl, either of which bears 0-3 substituents independently selected from halogen, CN, NO₂, CF₃, OH, OCF₃, C₁₋₄alkoxy or C₁₋₄alkyl which optionally bears a substituent selected from halogen, CN, NO₂, CF₃, OH and C₁₋₄alkoxy; and

Ar² represents C₆₋₁₀aryl or heteroaryl, either of which bears 0-3 substituents independently selected from halogen, CN, NO₂, CF₃, OH, OCF₃, C₁₋₄alkoxy or C₁₋₄alkyl which optionally bears a substituent selected from halogen, CN, NO₂, CF₃, OH and C₁₋₄alkoxy.

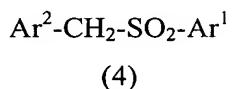
Claim 2 (Original) A method according to claim 1 wherein the cycloaddition reaction between the vinyl derivative (2b) and 2-trialkylsilyloxybutadiene (2a) to form silyl enol ether (3) is carried out at 100-150°C in a hydrocarbon solvent under an inert atmosphere.

Claim 3 (Amended) A method according to claim 1 or ~~claim 2~~ wherein hydrolysis of the silyl enol ether (3) to the cyclohexanone (1) is carried out *in situ* without isolation or further purification of the silyl enol ether.

Claim 4 (Original) A method according to claim 3 wherein said hydrolysis is carried out by treatment with aqueous mineral acid at 30-80°C.

Claim 5 (Amended) A method according to ~~any previous claim 1~~ wherein each R represents methyl.

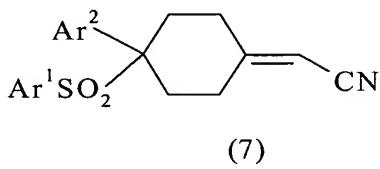
Claim 6 (Amended) A method according to ~~any previous claim 1~~ wherein the vinyl derivative (2) is prepared by reaction of a sulphone (4):



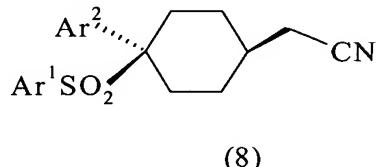
with N,N,N',N'-tetramethyldiaminomethane and acetic anhydride in DMF and Ar¹ and Ar² are as defined in claim 1.

Claim 7 (Amended) A method according to ~~any previous claim 1~~ comprising the additional steps of:

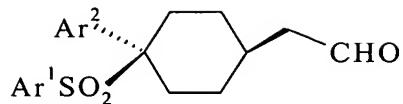
(c) reacting a cyclohexanone of formula (1) with a di(C₁₋₄alkyl) cyanomethylphosphonate and base to form a cyclohexylideneacetonitrile (7):



(d) reducing said cyclohexylideneacetonitrile with lithium tri-*sec*-butylborohydride to form the corresponding *cis* cyclohexaneacetonitrile (8):

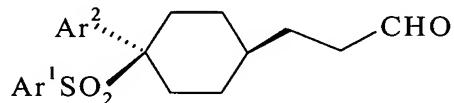


(e) sequential treatment of said *cis* cyclohexaneacetonitrile with diisobutylaluminium hydride and aqueous acid to form the corresponding *cis* cyclohexaneacetaldehyde (9):



(9)

(f) homologation of said *cis* cyclohexaneacetaldehyde to the corresponding *cis* cyclohexanepropanal (10):



(10)

and

(g) oxidising said *cis* cyclohexanepropanal to the corresponding *cis* cyclohexanepropanoic acid (6);

wherein Ar^1 and Ar^2 are as defined in claim 1 and “*cis*” refers to the stereoconfiguration of the side chain relative to the Ar^1SO_2 group.

Claim 8 (Original) A method according to claim 7 wherein in step (c) the C_{1-4} alkyl groups are ethyl, the reaction is carried out in THF at 0°C or below and the base is potassium *t*-butoxide.

Claim 9 (Amended) A method according to claim 7 or claim 8 wherein the reduction in step (d) is carried out in THF at about -60°C.

Claim 10 (Amended) A method according to ~~any of claims~~ claim 7 to 9 wherein the homologation in step (f) is effected by reaction of the *cis* cyclohexaneacetaldehyde (9) with a methoxymethyltriphenylphosphonium salt and strong base, followed by hydrolysis of the resulting mixture of enol ethers with aqueous acid.

Claim 11 (Amended) A method according to ~~any of claims~~ claim 7 to 10 comprising the additional step of neutralising the cyclohexanepropanoic acid (6) with sodium hydroxide to form the sodium salt thereof.

Claim 12 (Amended) A method according to ~~any previous claim~~ claim 1 wherein Ar^1 represents 4-chlorophenyl, 4-trifluoromethylphenyl or 6-trifluoromethylpyridin-3-yl and Ar^2 represents 2,5-difluorophenyl or 2,3,6-trifluorophenyl.

Claim 13 (Original) A method of preparing sodium *cis*-4-[(4-chlorophenyl)sulfonyl]-4-(2,5-difluorophenyl)cyclohexanopropanoate comprising the steps of:

- (i) preparing 4-[(4-chlorophenyl)sulfonyl]-4-(2,5-difluorophenyl)cyclohexanone by the method of claim 1 wherein Ar¹ represents 4-chlorophenyl and Ar² represents 2,5-difluorophenyl;
- (ii) reacting the product of step (i) with diethyl cyanomethylphosphonate and potassium *tert*-butoxide to form [4-[(4-chlorophenyl)sulfonyl]-4-(2,5-difluorophenyl)cyclohexylidene]-acetonitrile;
- (iii) reducing the product of step (ii) with lithium tri-*sec*-butylborohydride to form *cis*-4-[(4-chlorophenyl)sulfonyl]-4-(2,5-difluorophenyl)cyclohexaneacetonitrile;
- (iv) reacting the product of step (iii) sequentially with diisobutylaluminium hydride and with aqueous acid to form *cis*-4-[(4-chlorophenyl)sulfonyl]-4-(2,5-difluorophenyl)cyclohexanopropanal;
- (v) reacting the product of step (iv) with methoxymethyltriphenyl-phosphonium chloride and potassium *tert*-butoxide, then hydrolysing the resulting mixture of enol ethers with aqueous acid to form *cis*-4-[(4-chlorophenyl)sulfonyl]-4-(2,5-difluorophenyl)cyclohexanopropanal;
- (vi) oxidising the product of step (v) with aqueous sodium chlorite and sulphamic acid to form *cis*-4-[(4-chlorophenyl)sulfonyl]-4-(2,5-difluorophenyl)cyclohexanopropanoic acid; and
- (vii) neutralising the product of step (vi) with sodium hydroxide.